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(FILE 'HOME' ENTERED AT 16:25:19 ON 18 AUG 2003)

FILE 'CAPLUS' ENTERED AT 16:25:52 ON 18 AUG 2003

L1 367 S ((ALPHA(W)1) (W) (BETA(W)(1))) (2A) INTEGRIN
L2 161 S L1 AND BINDING
L3 17 S L2 AND PATENT/DT
L4 144 S L2 NOT L3
L5 144 SORT L4 PY
L6 47 S L1 (3A) BINDING
L7 46 S L6 NOT PATENT/DT

=> d bib,abs 25-46

L7 ANSWER 25 OF 46 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1999:568532 CAPLUS
DN 131:307971
TI Trench-shaped binding sites promote multiple classes of interactions between collagen and the adherence receptors, .alpha.1.beta.1 integrin and Staphylococcus aureus Cna MSCRAMM
AU Rich, Rebecca L.; Deivanayagam, Champion C. S.; Owens, Rick T.; Carson, Michael; Hook, Agneta; Moore, Dwight; Yang, Vivian W.-C.; Narayana, Sthanam, V. L.; Hook, Magnus
CS Center for Extracellular Matrix Biology, Institute of Biosciences and Technology, Texas A and M University, Houston, TX, 77030, USA
SO Journal of Biological Chemistry (1999), 274(35), 24906-24913
CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology
DT Journal
LA English
AB Most mammalian cells and some pathogenic bacteria are capable of adhering to collagenous substrates in processes mediated by specific cell surface adherence mols. Crystal structures of collagen-binding regions of the human integrin .alpha.2.beta.1 and a Staphylococcus aureus adhesin reveal a "trench" on the surface of both of these proteins. This trench can accommodate a collagen triple-helical structure and presumably represents the ligand-binding site. The authors report here the crystal structure of the .alpha. subunit I-domain from the .alpha.1.beta.1 integrin. This collagen-binding protein also contains a trench on one face in which the collagen triple helix may be docked. Furthermore, the authors compare the collagen-binding mechanisms of the human .alpha.1 integrin I domain and the A domain from the S. aureus collagen adhesin, Cna. Although the S. aureus and human proteins have unrelated amino acid sequences, secondary structure compn., and cation requirements for effective ligand binding, both proteins bind at multiple sites within one collagen mol., with the sites in collagen varying in their affinity for the adherence mol. The authors propose that (i) these evolutionarily dissimilar adherence proteins recognize collagen via similar mechanisms, (ii) the multisite, multiclass protein/ligand interactions obsd. in these two systems result from a binding-site trench, and (iii) this unusual binding mechanism may be thematic for proteins binding extended, rigid ligands that contain repeating structural motifs.
RE.CNT 58 THERE ARE 58 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 26 OF 46 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1998:532884 CAPLUS
DN 129:300278
TI Integrins--a versatile and old family of cell adhesion molecules
AU Eble, Johannes A.
CS Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA, USA
SO Integrin-Ligand Interaction (1997), 1-40. Editor(s): Eble, Johannes A.; Kuehn, Klaus. Publisher: Landes, Austin, Tex.

CODEN: 66OPAT
DT Conference; General Review
LA English
AB A review with 372 refs., on domain structure of integrins and integrin subunits; integrins as part of a supramol. structure in the cell membrane; integrins as receptors for extracellular matrix proteins; collagen-**binding integrins**, .**alpha.1**.
beta.1, .alpha.2.beta.1, and .alpha.9.beta.1;
.alpha.1.beta.1, mediation of cell-cell interactions; and integrins throughout the animal species.
RE.CNT 309 THERE ARE 309 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 27 OF 46 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1996:564965 CAPLUS
DN 125:219550
TI Functional analysis of .alpha.1.beta.1 integrin in human natural killer cells
AU Perez-Villar, Juan J.; Melero, Ignacio; Gismondi, Angela; Santoni, Angela; Lopez-Botet, Miguel
CS Servicio Inmunologia, Hospital Princesa, Madrid, Spain
SO European Journal of Immunology (1996), 26(9), 2023-2029
CODEN: EJIMAF; ISSN: 0014-2980
PB VCH
DT Journal
LA English
AB Upon activation with interleukin (IL)-2 human natural killer (NK) cells acquire on their surface the .alpha.1.beta.1 and .alpha.2.beta.1 integrins and down-regulate the expression of .alpha.6.beta.1. By employing .alpha.1.beta.1-specific monoclonal antibody (mAb) HP-2B6, characterized in our lab., we examd. the functional role of the .alpha.1.beta.1 integrin in NK cells. Treatment with HP-2B6 mAb partially interfered with attachment of cultured NK cells to type I collagen, and combined with an anti-.alpha.2.beta.1 (TEA 1/41) mAb, it completely abrogated cell adhesion to this extracellular matrix protein. In contrast, NK cell attachment to laminin was completely blocked by the anti-.beta.1 LIA 1/2 mAb, but was unaffected by .alpha.1 and .alpha.2-specific mAb; as .alpha.3.beta.1 and .alpha.6.beta.1 were undetectable, the data indicate that the .
alpha.1.beta.1 integrin
binding sites for type I collagen and laminin are different. Incubation with anti-.alpha.1 HP-2.beta.6 or its F(ab')2 fragments specifically induced a rapid homotypic aggregation of NK cells that was dependent on active metab., an intact cytoskeleton and the presence of divalent cations (Ca2+ and Mg2+); homotypic cell adhesion was selectively blocked by anti-CD18, CD11a or CD54 mAb. In addn., stimulation of cultured NK cells with the anti-.alpha.1 HP-2.beta.6 enhanced TNF-.alpha. prodn. and induced tyrosine phosphorylation of a 110-kDa protein. Pretreatment with specific inhibitors of protein tyrosine kinase (PTK) activity (tyrphostin 25 and herbimycin A) completely abrogated the functional effects induced by the anti-.alpha.1 HP-2B6 mAb. Our data show that ligation of the .alpha.1.beta.1 integrin pos. modulates IL-2-activated NK cell function via a PTK-dependent pathway.

L7 ANSWER 28 OF 46 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1996:312409 CAPLUS
DN 125:3997
TI Promotion of fibroblast adhesion by triple-helical peptide models of type I collagen-derived sequences
AU Grab, Beate; Miles, Andrew J.; Furcht, Leo T.; Fields, Gregg B.
CS Dep. Lab. Med. Pathol., Univ. Minnesota, Minneapolis, MN, 55455, USA
SO Journal of Biological Chemistry (1996), 271(21), 12234-12240
CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology
DT Journal

LA English
AB The dissection of the activities mediated by type I collagen requires an approach by which the influence of triple-helical conformation can be evaluated. The .alpha.1.beta.1 and .alpha.2.beta.1 integrin binding sites within type I collagen are dependent upon triple-helical conformation and contained within residues 124-822 from .alpha.1(I). Seven .alpha.1(I)-derived triple-helical peptides (THPs) were synthesized based on charge clustering (.alpha.1(I)256-270, .alpha.1(I)385-396, .alpha.1(I)406-417, .alpha.1(I)415-423, .alpha.1(I)448-456, .alpha.1(I)496-507, and .alpha.1(I)526-537). Three addnl. THPs were synthesized (.alpha.1(I)85-96, .alpha.1(I)433-441, and .alpha.1(I)772-786) based on previously described or proposed activities (Kleinmann, H . K., McGoodwin, E. B., Martin, G. R., Klebe, R. J., Fietzek, P. P., and Wooley, D. E. (1978) J. Biol. Chem. 253, 5642-5646; Staatz, W. D., Fok, K. F., Zutter, M. M., Adams, S. P., Rodriguez, B. A., and Santoro, S. A. (1991) J. Biol. Chem. 266, 7363-7367; San Antonio, J. D., Lander, A. D., Karnovsky, M. J., and Slayter, H. S. (1994) J. Cell Biol. 125, 1179-1188). Of the ten THPs, .alpha.1(I)772-786 THP had the greatest activity, with half-maximal normal dermal fibroblast adhesion occurring at a peptide concn. of 1.6 .mu.M. Triple-helicity was essential for activity of this sequence, as the non-triple-helical peptide analog (.alpha.1(I)772-786 SSP) exhibited considerably lower levels of cell adhesion promotion even at peptide concns. as high as 100 .mu.M. Within the sequence itself, residues 784-786 (Gly-Leu-Hyp) were important for cellular recognition, as the .alpha.1(I)772-783 THP had greatly reduced cell adhesion activity compared with .alpha.1(I)772-786 THP. Preliminary studies indicate that the .beta.1 integrin subunit mediates fibroblast adhesion to .alpha.1(I)772-786 THP. The identification of fibroblast integrin binding sites within type I collagen may have important implications for understanding collagen metab.

L7 ANSWER 29 OF 46 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1995:974735 CAPLUS
DN 124:26891
TI Chondrocyte and chondrosarcoma cell integrins with affinity for collagen type II and their response to mechanical stress
AU Holmvall, Karin; Camper, Lisbet; Johansson, Staffan; Kimura, James H.; Lundgren-Aakerlund, Evy
CS Dep. Cell Mol. Bioloy, Univ. Lund, Swed.
SO Experimental Cell Research (1995), 221(2), 496-503
CODEN: ECREAL; ISSN: 0014-4827
PB Academic
DT Journal
LA English
AB Mech. stress is an important regulator of chondrocyte functions but the mechanisms by which chondrocytes sense mech. signaling. In the first part of this study we identified integrins with affinity for the cartilage-specific collagen type II. We report that the collagen-**binding integrins .alpha.1.beta.1** and .alpha.2.beta.1 isolated from bovine chondrocytes or human chondrosarcoma cells bound collagen type II as judged from affinity chromatog. The integrins .alpha.3.beta.1 or .alpha.9.beta.1 did not bind collagen type II-Sepharose. In the second part of the study we investigated the effect of mech. stress on expression of matrix mols. and integrin subunits. Chondrocytes and chondrosarcoma cells, cultured on uncoated flexible silicone membranes in the presence of serum, were exposed to mech. stress by the Flexercell system. Dynamic stimulation of chondrocytes for 3 h increased the mRNA expression of collagen type II and aggrecan as judged by Northern blotting, while the .beta.1-integrin subunit was not changed. When chondrosarcoma cells were exposed to mech. stimulation under the same conditions, mRNA expression of .alpha.5 was found to increase while .beta.1, .alpha.2, and .alpha.v did not increase to significant levels. In another study the effect of mech. stress on integrins was investigated when the cells were cultured on

collage type II-coated flex-dishes. Three hours of dynamic stress increased the mRNA expression of .alpha.2-integrin subunit while the level of mRNA for integrin subunits .beta.1, .alpha.1, .alpha.5, and .alpha.v showed no or small changes, indicating that matrix components may modulate the expression of integrins during mech. stress.

L7 ANSWER 30 OF 46 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1995:609228 CAPLUS
DN 123:194705
TI Integrin .alpha.2.beta.1 is a positive regulator of collagenase (MMP-1) and collagen .alpha.1(I) gene expression
AU Riikonen, Terhi; Westermarck, Jukka; Koivisto, Leeni; Broberg, Arsi; Kaehaeri, Veli-Matti; Heino, Jyrki
CS MediCity Res. Lab., Univ. Turku, Turku, FIN-20520, Finland
SO Journal of Biological Chemistry (1995), 270(22), 13548-52
CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology
DT Journal
LA English
AB A classical model for studying the effects of extracellular matrix is to culture cells inside a three-dimensional collagen gel. When surrounded by fibrillar collagen, many cell types decrease the prodn. of type I collagen, and the expression of interstitial collagenase (matrix metalloproteinase-1; MMP-1) is simultaneously induced. To study the role of the collagen-**binding integrins .alpha.1.beta.1** and .alpha.2.beta.1 in this process, the authors used three different osteogenic cell lines with distinct patterns of putative collagen receptors: HOS cells, which express only .alpha.1.beta.1 integrin, MG-63 cells, which express only .alpha.2.beta.1 integrin, and KHOS-240 cells, which express both. Inside collagen gels, .alpha.1(I) collagen mRNA levels were decreased in HOS and KHOS-240 cells but not in MG-63 cells. In contrast, MMP-1 expression was induced in KHOS-240 and MG-63 cells but not in HOS cells. Transfection of MG-63 cells with .alpha.2 integrin cDNA produced cell clones overexpressing .alpha.2.beta.1 integrin. Transfection of MG-63 cells with .alpha.2 integrin cDNA in an antisense orientation reduced the expression level of .alpha.2 integrin. These cell clones showed induction and redn., resp., of mRNA levels for MMP-1. HOS cells normally lacking .alpha.2.beta.1 integrin were forced to express it, and this prevented the down-regulation in the levels of .alpha.(I) collagen mRNA when cells were grown inside collagen gels. The data indicate that the level of MMP-1 expression is regulated by the collagen receptor .alpha.2.beta.1 integrin. The down-regulation of collagen .alpha.1(I) is mediated by another receptor. Integrin .alpha.2.beta.1 may compete with it and thus be a pos. regulator of collagen synthesis.

L7 ANSWER 31 OF 46 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1995:522068 CAPLUS
DN 122:309154
TI Mapping of network-forming, heparin-**binding**, and .**alpha**.**1**.**beta**.**1 integrin**-recognition sites within the .alpha.-chain short arm of laminin-1
AU Colognato-Pyke, Holly; O'Rear, Julian J.; Yamada, Yoshihiko; Carbonetto, Salvatore; Cheng, Yi-Shan; Yurchenco, Peter D.
CS Dep. Pathol. Microbiol. Mol. Genetics, Robert Wood Johnson Med. Sch., Piscataway, NJ, 08854, USA
SO Journal of Biological Chemistry (1995), 270(16), 9398-406
CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology
DT Journal
LA English
AB Cell-interactive and architecture-forming functions are assocd. with the short arms of basement membrane laminin-1. To map and characterize these functions, the authors expressed recombinant mouse laminin-1 .alpha.-chain

extending from the N terminus through one third of domain IIIb. This dumbbell-shaped glycoprotein (r.alpha.1(VI-IVb)'), secreted by mammalian cells, was found to possess three activities. (1) Laminin polymn. was quant. inhibited by recombinant protein, supporting an .alpha.-chain role for a three-short arm interaction model of laminin self-assembly. (2) R.alpha.1(VI-IVb)' bound to heparin, and the activity was localized to a subfragment corresponding to domain VI by 125I-heparin blotting. (3) PC12 rat pheochromocytoma cells adhered to, and rapidly extended branching neurites on, r.alpha.1(VI-IVb)', with adhesion inhibited by .alpha.1 and .beta.1 integrin chain-specific antibodies. The ability of anti-laminin antibody to block PC12 cell adhesion to laminin was selectively prevented by absorption with r.alpha.1(VI-IVb)' or .alpha.-chain domain VI fragment. This active integrin-recognition site could furthermore be distinguished from a second cryptic .alpha.1.beta.1-binding site exposed by heat treatment of fragment P1', a short arm fragment lacking globules. Thus, a polymer-forming, a heparin-**binding**, and the active .
alpha.1.beta.1 integrin
-recognition site are all clustered at the end of the .alpha.-chain short arm, the latter two resident solely in domain VI.

L7 ANSWER 32 OF 46 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1995:411976 CAPLUS
DN 122:210506
TI Differential expression of collagen-binding receptors in fetal rat lung cells
AU Caniggia, Isabella; Han, Robin; Liu, Jason; Wang, Jinxia; Tanswell, A. Keith; Post, Martin
CS Department of Pediatrics, Hospital for Sick Children Research Institute, Toronto, ON, M5G 1X8, Can.
SO American Journal of Physiology (1995), 268(1, Pt. 1), L136-L143
CODEN: AJPHAP; ISSN: 0002-9513
PB American Physiological Society
DT Journal
LA English
AB Interactions of cells with mols. of the extracellular matrix (ECM) are mediated via specific cell surface receptors. Because collagen is an important ECM component in the developing lung, the authors investigated the expression of collagen receptors by distal fetal lung epithelial cells and fibroblasts. Cell attachment expts. revealed that fibroblasts but not epithelial cells adhered to various types of collagen. With the use of subunit-specific antibodies, the authors demonstrated the presence of the collagen integrins .alpha.1.beta.1, .alpha.2.beta.1, and .alpha.3.beta.1 at the fibroblast surface but only the integrin .alpha.3.beta.1 on epithelial cells. Affinity chromatog. on collagen-Sepharose identified only .alpha.1.beta.1 and .alpha.2.beta.1 as collagen-binding integrins in exts. of 125I surface-labeled fibroblasts. No collagen-binding receptors were detected in exts. of surface-iodinated epithelial cells. Message for .alpha.1- and .alpha.2-integrin was readily demonstrated for fibroblasts, but both mRNAs were hardly detectable in epithelial cells. In contrast, epithelial cells expressed significantly greater .alpha.3 mRNA levels than fibroblasts. These data demonstrate that .alpha.1.beta.1- and .alpha.2.beta.1-integrins function as collagen-binding receptors in fetal lung fibroblasts. Distal fetal lung epithelial cells do not express the .alpha.1.beta.1- and .alpha.2.beta.1-integrins and do not adhere to collagen. The .alpha.3.beta.1-integrin, which is expressed by both cell types, does not function as a collagen receptor.

L7 ANSWER 33 OF 46 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1995:298848 CAPLUS
DN 122:77769
TI Selective increase in the **binding** of the .**alpha**.
1.beta.1 integrin for collagen type
IV during neurite outgrowth of human neuroblastoma TR 14 cells
AU Carmeliet, Geert; Himpens, Bernard; Cassiman, Jean Jacques

CS Cent. Human Genetics, Univ. Leuven, Leuven, B-3000, Belg.
SO Journal of Cell Science (1994), 107(12), 3379-92
CODEN: JNCSAI; ISSN: 0021-9533
PB Company of Biologists
DT Journal
LA English
AB Regulation of .beta.1 integrins in neurite outgrowth following N6,2'-O-dibutyryladenosine 3':5'-cyclic monophosphate (dBcAMP) treatment was investigated using the human neuroblastoma cell line TR 14. Three .beta.1 integrins were identified: the .alpha.1.beta.1 receptor bound collagen type I, collagen type IV and probably laminin; the .alpha.2.beta.1 integrin bound collagen type I; and the .alpha.v.beta.1 receptor bound fibronectin. Neurite extension was detectable as early as 30 min following dBcAMP treatment, was maximal after 24 h and remained const. during treatment for 4 days. Adhesion-perturbing .beta.1 subunit-specific antibodies, added together with dBcAMP, prevented the outgrowth of new neurites. During the first 24 h of neurite outgrowth, no change was obsd. in the amt. of .beta.1 integrins nor in their topog. distribution. However, dBcAMP treatment increased the binding of .alpha.1.beta.1 receptors to collagen type IV-Sepharose by a factor 2.3 .+-. 0.6 (P<0.02), while no alteration in the binding to collagen type I was detected. Moreover, neurites and growth cones were immunoreactive for collagen type IV but not for collagen type I. Consistently, dBcAMP-induced neurite outgrowth was inhibited by adhesion-perturbing .alpha.1 subunit-specific antibodies. Following maximal neurite outgrowth, the amt. of .beta.1 integrins detd. by immunopptn. and by confocal microscopy decreased to 58.3 .+-. 11.2% (P<0.001) and to 55.4 .+-. 17.5% (P<0.001) of untreated levels, resp., without any change in the level of .beta.1 mRNA or de novo synthesized .beta.1 precursor. However, pulse-chase expts. showed an increased turnover of the .beta.1 subunit: the amt. of .beta.1 precursor that was degraded after 1 h chase was 50.5 .+-. 8.4% in cells treated for 4 days and 34.2 .+-. 3.9% in untreated cells (P>0.02); the amt. of mature .beta.1 after 24 h chase was smaller in cells treated for 4 days compared to untreated cells. In conclusion, during neurite outgrowth, .alpha.1.beta.1 integrins are required and acquire an enhanced binding activity for collagen type IV; but following maximal neurite outgrowth, expression of .beta.1 integrins is reduced.

L7 ANSWER 34 OF 46 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1994:677525 CAPLUS
DN 121:277525
TI Laminin isoforms promote attachment of hepatocytes via different integrins
AU Forsberg, E.; Lindblom, A.; Paulsson, M.; Johansson, S.
CS Department of Medical and Physiological Chemistry, University of Uppsala, Uppsala, S-751 23, Swed.
SO Experimental Cell Research (1994), 215(1), 33-9
CODEN: ECREAL; ISSN: 0014-4827
DT Journal
LA English
AB Three isoforms of laminin were compared for the ability to promote adhesion of primary rat hepatocytes. In tests of initial attachment to these substrates, kidney laminin (.alpha.k,.beta.1,.gamma.1, and .alpha.k,.beta.2,.gamma.1) was shown to be a more efficient substrate than Engelbreth Holm Swarm (EHS) (.alpha.1,.beta.1,.gamma.1) or heart laminin (.alpha.2,.beta.1,.gamma.1, and .alpha.2,.beta.2,.gamma.1). Hepatocyte attachment to EHS laminin and heart laminin was completely inhibited by antibodies specific for the integrin subunit .beta.1, while a combination of .beta.1 integrin antibodies and GRGDS peptide was needed for total inhibition of hepatocyte attachment to kidney laminin. Antiserum directed to the integrin subunit .beta.3 could not substitute for the GRGDS peptide in this inhibition. Antibodies against the integrin subunit .alpha.1 efficiently blocked adhesion of hepatocytes to collagen type I and to the P1 domain of EHS laminin. However, this antibody had essentially no effect on the attachment to kidney laminin and had only a minor inhibitory

effect on attachment to heart laminin, to intact EHS laminin, or to the isolated fragment E8 of EHS laminin. Combining the .alpha.1 integrin antibody with GRGDS peptide gave no further inhibition on these substrates. These results show that a recently described isoform of laminin from bovine kidney is an efficient substrate for initial attachment of hepatocytes, interacting with at least one .beta.1-contg. integrin and an RGD-dependent integrin not contg. .beta.1 or .beta.3 subunits. Native EHS laminin uses **integrin .alpha.1.beta.1** for hepatocyte **binding** to the center of the cross (fragment P1) and other .beta.1 integrin(s) in addn. to .alpha.1.beta.1 as receptors for the distal part of the long arm (fragment E8).

L7 ANSWER 35 OF 46 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1994:674719 CAPLUS
DN 121:274719
TI The role of the I domain in ligand **binding** of the human **integrin .alpha.1.beta.1**
AU Kern, Andreas; Briesewitz, Roger; Bank, Ilan; Marcantonio, Eugene E.
CS Coll. Physicians and Surgeons, Columbia Univ., New York, NY, 10032, USA
SO Journal of Biological Chemistry (1994), 269(36), 22811-16
CODEN: JBCHA3; ISSN: 0021-9258
DT Journal
LA English
AB We report here the anal. of potential ligand binding domains within the human integrin .alpha.1 subunit, a known collagen/laminin receptor. This integrin is effectively blocked by the mouse monoclonal antibody 1B3.1. A truncated version of the .alpha.1 subunit lacking the NH2-terminal half of the extracellular domain is not recognized by monoclonal antibody 1B3.1. Furthermore, we have isolated a cDNA contg. the I domain from chicken .alpha.1 bearing significant homol. to the human and rat .alpha.1 sequences. Replacing the human I domain with its chicken counterpart led to the surface expression of a functional heterodimer with endogenous mouse .beta.1 on NIH 3T3 cells. However, 1B3.1 does not bind to the chicken/human chimera, demonstrating that the human .alpha.1 I domain is required for epitope recognition. Mutation of Asp253 within the I domain to alanine resulted in surface expression of an .alpha..beta. heterodimer recognized by 1B3.1 but with markedly reduced binding to collagen IV or laminin. Since a previously reported mutation of a homologous Asp in the Mac-1 I domain has similar consequences, these results suggest a central role for the I domain in ligand recognition for all integrin a subunits contg. this domain.

L7 ANSWER 36 OF 46 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1994:648881 CAPLUS
DN 121:248881
TI Binding of purified collagen receptors (.alpha.1.beta.1, .alpha.2.beta.1) and RGD-dependent integrins to laminins and laminin fragments
AU Pfaff, Martin; Goehring, Walter; Brown, Judith C.; Timple, Rupert
CS Max-Planck-Inst. Biochem., Martinsried, Germany
SO European Journal of Biochemistry (1994), 225(3), 975-84
CODEN: EJBCAI; ISSN: 0014-2956
PB Springer
DT Journal
LA English
AB Integrins .alpha.1.beta.1 and .alpha.2.beta.1, when purified by collagen affinity chromatog., showed distinct binding to mouse tumor laminin-1, which has the chain compn. .alpha.1.beta.1.gamma.1. The binding was, however, about 10-fold lower than to collagen IV. Only little (.alpha.1.beta.1) or no binding (.alpha.2.beta.1) was obsd. to two different laminin isoforms (.alpha.2.beta.1.gamma.1, .alpha.2.beta.2.gamma.1) from human placenta. Binding to laminin-1 was abolished by EDTA and could be specifically inhibited by antibodies to the resp. integrin .alpha. subunit. These antibodies also inhibited cell

adhesion to collagens. The binding of sol. integrins was weaker than that of immobilized integrins but could be enhanced by an activating anti(.beta.1 integrin). No enhancement was obsd. for immobilized integrins. Studies with laminin-1 fragments demonstrated lack of binding to the major cell-adhesive fragment E8 from the long arm, fragments E3 and E4, involved in heparin-binding and self-assembly, resp., and fragment P1, corresponding to the inner segments of the short arms. A larger short-arm fragment (E1XNd), which lacks the N-terminal .beta.1 chain domains V and VI, was as active as laminin. Together, these results, suggested the localization of the binding sites for .alpha.1.beta.1 and .alpha.2.beta.1 to the N-terminal region of the laminin .alpha.1 chain. Fragment P1 but not intact laminin-1 bound to .alpha.V.beta.3 integrin in an EDTA-sensitive and RGD-sensitive manner, underscoring previous data on the cryptic nature of the RGD site in laminin-1. Further analyses by surface plasmon resonance assays demonstrated a KD = 50 nM for .alpha.2.beta.1/laminin-1 binding and a KD = 450 nM for .alpha.V.beta.3/fragment P1 binding and confirmed the anti-.beta.1-mediated increase in affinity for .alpha.2.beta.1.

L7 ANSWER 37 OF 46 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1994:601711 CAPLUS
DN 121:201711
TI Cell adhesion receptors for native and denatured type I collagens and fibronectin in rabbit arterial smooth muscle cells in culture
AU Yamamoto, Kiyotaka; Yamamoto, Mari
CS Department of Cell Biology, Tokyo Metropolitan Institute of Gerontology, Tokyo, 173, Japan
SO Experimental Cell Research (1994), 214(1), 258-63
CODEN: ECREAL; ISSN: 0014-4827
DT Journal
LA English
AB Cell adhesion mols. serve as specific cell surface receptors for extracellular matrixes and contribute to the attachment, spreading, proliferation, and differentiation of vascular cells. The authors examd. the cell adhesion receptors and binding sites on native type I adhesion receptors and binding sites on native type I collagen, heat-denatured type I collagen, and fibronectin in rabbit arterial smooth muscle cells (SMC) in culture. On fibronectin, anti-.alpha.3.beta.1 and anti-.alpha.5.beta.1 integrin antibodies and the synthetic peptide GRGDSP significantly inhibited the attachment and spreading of rabbit SMC after 1 and 24 h of culture, while anti-.alpha.1.beta.1 inhibited attachment and spreading only after 1 h. In contrast, the attachment and spreading of the cells on native type I collagen were mediated by .**alpha.1**. **beta.1 integrin** and the cell-**binding** sequence which did not contain RGD and DGEA after both 1 and 24 h. On heat-denatured type I collagen, .alpha.2.beta.1 integrin mediated the cell attachment and spreading after 1 and 24 h and DGEA served as a recognition site for the .alpha.2.beta.1 integrin. .alpha.1.beta.1 And .alpha.3.beta.1 integrins affected only the initial adherence (1 h after plating) of the cells to denatured type I collagen. These findings suggest that rabbit SMC in culture can recognize the native and unfolded triple helical structures of type I collagen by interacting with the collagen fibril-**binding** receptor (.**alpha.1**. **beta.1 integrin**) and collagen peptide-**binding** receptors (.alpha.2.beta.1 and .alpha.3.beta.1 integrins). Moreover, .alpha.1.beta.1 integrin may mediate the initial adherence to each substrate.

L7 ANSWER 38 OF 46 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1994:319724 CAPLUS
DN 120:319724
TI Neural crest cell interactions with laminin: structural requirements and localization of the **binding** site for .**alpha.1** .**beta.1 integrin**

AU Lallier, Thomas; Deutzmann, Rainer; Perris, Roberto; Bronner-Fraser, Marianne
CS Dev. Biol. Cent., Univ. California, Irvine, CA, 92717, USA
SO Developmental Biology (Orlando, FL, United States) (1994), 162(2), 451-64
CODEN: DEBIAO; ISSN: 0012-1606
DT Journal
LA English
AB The authors have identified the sites of neural crest cell interaction with laminin in vitro by examg. their ability to attach to and migrate on proteolytic fragments of the mol. and the ability of fragment-specific antibodies to inhibit these interactions. The binding site on laminin was localized to the E8 domain on the long arm of laminin, as well as the T8' fragment within this domain, but not the E1', E3, or E4 fragments. Only subfragments contg. the carboxy-terminal rod-like portion of the A chain plus the corresponding B1 and B2 chains retained the attachment-promoting activity of the parent E8 fragment. In addn., interactions required maintenance of the triple-stranded and .alpha.-helical coiled-coil structure of this domain. Redn. and alkylation of laminin and the E8 and T8 fragments significantly reduced neural crest cell attachment and migration. An antiserum against chick .alpha.1 integrin reduced migration and adhesion of neural crest cells on an intact laminin-nidogen complex, the E8 fragment, and all its active subfragments. Furthermore, the authors obsd. that neural crest cells modified laminin substrate prepd. in the absence of divalent cations. Early stable attachment to these substrate was mediated by an integrin other than .alpha.1, whereas later attachment and migration were mediated by .alpha.1 integrins. The authors' results suggest that neural crest cells selectively bind to the B1-A-B2 mid-portion (T8') of the E8 domain of laminin, requiring structural integrity of this region and that they modify laminin substrate as a result of prolonged cell-matrix interactions.

L7 ANSWER 39 OF 46 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1994:294542 CAPLUS
DN 120:294542
TI Molecular mechanisms of neural crest cell attachment and migration on types I and IV collagen
AU Perris, Roberto; Syfrig, Josef; Paulsson, Mats; Bronner-Fraser, Marianne
CS Exp. Div., Ref. Cent. Oncol., Aviano, 33081, Italy
SO Journal of Cell Science (1993), 106(4), 1357-68
CODEN: JNCSAI; ISSN: 0021-9533
DT Journal
LA English
AB The authors have examd. the mechanisms involved in the interaction of avian neural crest cells with collagen types I and IV (Col I and IV) during their adhesion and migration in vitro. For this purpose native Col IV was purified from chicken tissues, characterized biochem. and ultrastructurally. Purified chicken Col I and Col IV, and various proteolytic fragments of the collagens, were used in quant. cell attachment and migration assays in conjunction with domain-specific collagen antibodies and antibodies to avian integrin subunits. Neural crest cells do not distinguish between different macromol. arrangements of Col I during their initial attachment, but do so during their migration, showing a clear preference for polymeric Col I. Interaction with Col I is mediated by the **.alpha.1.beta.1 integrin**, through **binding** to a segment of the .alpha.1(I) chain composed of fragment CNBr3. Neural crest cell attachment and migration on Col IV involves recognition of conformation-dependent sites within the triple-helical region and the noncollagenous, carboxyl-terminal NC1 domain. This recognition requires integrity of inter- and intrachain disulfide linkages and correct folding of the mol. Moreover, there also is evidence that interaction sites within the NC1 domain may be cryptic, being exposed during migration of the cells in the intact collagen as a result of the prolonged cell-substratum contact. In contrast to Col I, neural crest cell

interaction with Col IV is mediated by .beta.1-class integrins other than .alpha.1.beta.1.

L7 ANSWER 40 OF 46 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1994:25717 CAPLUS
DN 120:25717
TI The .alpha.1.beta.1 integrin recognition site of the basement membrane collagen molecule [.alpha.1(IV)]2.alpha.2(IV)
AU Eble, J. A.; Golbik, R.; Mann, K.; Kuehn, K.
CS Max-Planck-Inst. Biochem., Martinsried, 82152, Germany
SO EMBO Journal (1993), 12(12), 4795-802
CODEN: EMJODG; ISSN: 0261-4189
DT Journal
LA English
AB Cells interact with type IV collagen mainly via the integrins .alpha.1.beta.1 and .alpha.2.beta.1. A triple helical CNBr derived fragment CB3[IV], which contains the recognition sites for both integrins, was isolated from type IV collagen. Trypsin treatment of CB3[IV] gave rise to four smaller fragments, F1-F4, of which the smallest one, F4, contained the recognition site for .alpha.1.beta.1. Further fragmentation of F4 by thermolysin treatment at 50.degree.C led to fragment TL1, which represents the C-terminal half of F4, and which was no longer able to interact with .alpha.1.beta.1. Therefore the recognition site of .alpha.1.beta.1 had to be located within the N-terminal half of F4, a position which was verified by electron micrographs of a crosslinked F2-.alpha.1.beta.1 complex. Modification of the Arg and Asp residues, which abolished the binding activity of F4, led to the identification of Arg (461) within the .alpha.2(IV) and Asp (461) within the .alpha.1(IV) chain as essential residues for the .alpha.1.beta.1. The array of these two residues on the surface of the triple helix is discussed.

L7 ANSWER 41 OF 46 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1993:623389 CAPLUS
DN 119:223389
TI Impaired regulation of collagen pro-.alpha.1(I) mRNA and change in pattern of collagen-binding integrins on scleroderma fibroblasts
AU Ivarsson, Mikael; McWhirter, Alan; Black, Carol M.; Rubin, Kristofer
CS Dep. Med. Physiol. Chem., Univ. Uppsala, Uppsala, S-751 23, Swed.
SO Journal of Investigative Dermatology (1993), 101(2), 216-21
CODEN: JIDEAE; ISSN: 0022-202X
DT Journal
LA English
AB The authors explored the hypothesis that dermal fibroblasts isolated from patients suffering from systemic sclerosis are disturbed in their ability to interact functionally with native collagen fibers. Addnl., the authors investigated the expression of one collagen-**binding integrin** matrix receptor, .**alpha.1**.**beta.1** on those cells. Two populations of primary dermal fibroblasts were established, one from patients with systemic sclerosis and one from normal subjects. When cultured for 24 h in free-floating collagen gels, both types of fibroblasts down-regulated the cellular content of collagen pro-.alpha.1(I) mRNA, the systemic sclerosis fibroblasts less markedly than the normals. In normal, but not in systemic sclerosis fibroblasts, the kinetics of collagen gel contraction were directly proportional to the extent of the down-regulation. Fetal bovine serum stimulated collagen gel contraction in both populations. When grown in collagen gels in the presence of fetal bovine serum, no difference between systemic sclerosis and normal fibroblasts in capacity to down-regulate pro-.alpha.1(I) was obsd. Collagen-binding .beta.1 integrins mediate the functional interactions between fibroblasts and the collagen fibers. To assess the cell surface expression of collagen-binding .beta.1 integrins on fibroblasts, the authors labeled cells with 125I and subjected Triton X-100 exts. from them to immunopptn. with anti-.beta.1 integrin IgG. Among the systemic sclerosis fibroblasts,

a larger no. of isolates expressed a lower amt. of .alpha.1.beta.1 than did the fibroblasts isolated from normal individuals. The authors' data are compatible with the hypothesis that systemic sclerosis fibroblasts have a disturbed interaction with collagen fibers; this disturbance may in part be the result of an aberrant expression of collagen-binding .beta.1 integrins.

L7 ANSWER 42 OF 46 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1993:492157 CAPLUS
DN 119:92157
TI Integrin and Arg-Gly-Asp dependence of cell adhesion to the native and unfolded triple helix of collagen type VI
AU Pfaff, Martin; Aumailley, Monique; Specks, Ulrich; Knolle, Joachim; Zerwes, Hans Guenter; Timpl, Rupert
CS Max-Planck-Inst. Biochem., Martinsried, W-8033, Germany
SO Experimental Cell Research (1993), 206(1), 167-76
CODEN: ECREAL; ISSN: 0014-4827
DT Journal
LA English
AB Pepsin-solubilized collagen VI in triple-helical and heat-denatured, unfolded form was shown to promote Mg2+- and Mn2+-dependent attachment and spreading of various cell lines. On the triple-helical substrate no inhibition of cell adhesion was obsd. with several synthetic RGD peptides except in the case of A375 melanoma cells. In contrast, adhesion to the unfolded substrate was highly sensitive to RGD inhibition. Nine synthetic peptides were designed according to 10 RGD sequences present in the triple-helical sequence of human collagen .alpha.1(VI), .alpha.2(VI), and .alpha.3(VI) chains. Only one peptide, corresponding to the C-terminal end of .alpha.3(VI) chain, showed substantial inhibitory activity, whereas several peptides were active in direct adhesion assays when used as albumin conjugates. Inhibition tests with antibodies to integrin subunits, affinity chromatog., and ligand **binding** with purified **integrins** (.**alpha**.**1**.**beta**.**1**, .alpha.2.beta.1, .alpha.V.beta.3, and .alpha.IIb.beta.3) were used to identify collagen VI receptors. Binding to the triple-helical substrate is mediated by .alpha.1.beta.1 and .alpha.2.beta.1 integrins. Binding of both integrins to collagen VI was weaker than that to collagens I and/or IV. Recognition of the denatured substrate is mediated by .beta.1 and .beta.3 integrins. Activity was shown for .alpha.5.beta.1 and .alpha.V.beta.3 and weakly for .alpha.IIb.beta.3, but not all .alpha. subunits possibly involved were identified. Distinct sets of receptors were also involved in A375 cell binding to triple-helical (.beta.1-mediated) and denatured (.beta.3-mediated) collagen VI, even though in this case both interactions could be efficiently inhibited by RGD peptides.

L7 ANSWER 43 OF 46 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1993:489427 CAPLUS
DN 119:89427
TI Interaction of type IV collagen with the isolated integrins .alpha.1.beta.1 and .alpha.2.beta.1
AU Kern, Andreas; Eble, Johannes; Golbik, Ralph; Kuehn, Klaus
CS Max-Planck-Inst. Biochem., Martinsried, W-8033, Germany
SO European Journal of Biochemistry (1993), 215(1), 151-9
CODEN: EJBCAI; ISSN: 0014-2956
DT Journal
LA English
AB The triple-helical cyanogen-bromide-derived fragment CB3[IV] of collagen IV, located 100 nm from the N-terminus of the mol., contains the **binding** sites for the **integrins** .**alpha**.**1**.**beta**.**1** and .alpha.2.beta.1. To investigate the interaction of these integrins and collagen IV, solid-phase and inhibition assays using as receptor isolated .alpha.1.beta.1 and .alpha.2.beta.1 was performed. The ligands used were the

binding-site-bearing trimeric peptide CB3[IV] and its shorter tryptic fragments E1-E4. Using titrn. curves, in which the binding of sol. receptors to coated ligands and the binding of sol. ligands to coated receptors were analyzed, the binding sites for .alpha.1.beta.1 and .alpha.2.beta.1 were in different but adjacent areas of CB3[IV]. Triple-helical conformation and distinct primary structures were required for the interaction. Dissocn. consts. (Kd), for the affinity of integrins for collagen IV, were detd. in the 1 nM range in the presence of Mn2+ and Mg2+. In the absence of Mn2+, the Kd values indicated a 30-60 fold decrease in the affinities, which for .alpha.2.beta.1 was further reduced by adding Ca2+. In the presence of Ca2+ and Mg2+ the affinity of collagen IV for .alpha.1.beta.1 was four-times higher than for .alpha.2.beta.1.

L7 ANSWER 44 OF 46 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1992:631027 CAPLUS
DN 117:231027
TI Analysis of .alpha.1.beta.1, .alpha.2.beta.1 and .alpha.3.beta.1 integrins in cell-collagen interactions: identification of conformation dependent .alpha.1.beta.1 binding sites in collagen type I
AU Gullberg, Donald; Gehlsen, Kurt R.; Turner, David C.; Aahlen, Karina; Zijenah, Lynn S.; Barnes, Michael J.; Rubin, Kristofer
CS Dep. Med. Physiol. Chem., Uppsala Univ., Uppsala, S-751 23, Swed.
SO EMBO Journal (1992), 11(11), 3865-73
CODEN: EMJODG; ISSN: 0261-4189
DT Journal
LA English
AB The possible differences in collagen type I recognition sites for the .alpha.1.beta.1 and .alpha.2.beta.1 integrins were investigated. Different cyanogen bromide (CB) fragments of the .alpha.1(I) collagen chain were used in cell attachment expts. with 3 rat cell types, defined with regard to expression of collagen-binding integrins. Primary rat hepatocytes expressed .alpha.1.beta.1, primary rat cardiac fibroblasts .alpha.1.beta.1 and .alpha.2.beta.1, and Rat-1 cells only .alpha.2.beta.1. All 3 cell types expressed .alpha.3.beta.1, but this integrin did not bind to collagen-Sepharose or to immobilized collagen type I in a radioreceptor assay. Hepatocytes and cardiac fibroblasts attached to substrata coated with .alpha.1(I)CB3 and .alpha.1(I)CB8; Rat-1 cells attached to .alpha.1(I)CB3 but only poorly to .alpha.1(I)CB8-coated substrata. Cardiac fibroblasts and Rat-1 cells spread and formed .beta.1-integrin-contg. focal adhesions when grown on substrata coated with native collagen or .alpha.1(I)CB3; focal adhesions were also detected in cardiac fibroblasts cultured on .alpha.1(I)CB8. The rat .alpha.1-specific monoclonal antibody 3A3 completely inhibited hepatocyte attachment to .alpha.1(I)CB3 and .alpha.1(I)CB8, as well as the attachment of cardiac fibroblasts to .alpha.1(I)CB8, but only partially inhibited the attachment of cardiac fibroblasts to .alpha.1(I)CB3. 3A3 IgG did not inhibit the attachment of Rat-1 cells to collagen type I or to .alpha.1(I)CB3. These data indicate that binding sites for .alpha.1.beta.1 are present in both .alpha.1(I)CB3 and .alpha.1(I)CB8 and that .alpha.1(I)CB3, but not .alpha.1(I)CB8, contains a binding site for .alpha.2.beta.1, and suggest that collagen type I contains sep. binding sites for .alpha.1.beta.1 and .alpha.2.beta.1. Hepatocyte attachment to heat-denatured collagen type I was inhibited by the hexapeptide GRGDTP. It therefore appears that denaturation both destroys the integrity of conformation-dependent binding sites for .alpha.1.beta.1 and reveals a cryptic RGD-contg. site recognized by the .alpha.5.beta.1 of hepatocytes.

L7 ANSWER 45 OF 46 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1991:553426 CAPLUS
DN 115:153426
TI Affinity of integrin .alpha.1.beta.1 from liver sinusoidal membranes for type IV collagen
AU Stamatoglou, Stamatis C.; Bawumia, Sulemana; Johansson, Staffan; Forsberg, Erik; Hughes, R. Colin

CS Natl. Inst. Med. Res., London, NW7 1AA, UK
SO FEBS Letters (1991), 288(1-2), 241-3
CODEN: FEBLAL; ISSN: 0014-5793
DT Journal
LA English
AB Hepatic sinusoidal membranes isolated from adults rats were extd. with detergent and fractionated on a wheat germ agglutinin affinity column. Bound glycoproteins were eluted with N-acetylglucosamine and chromatographed on a type IV collagen affinity column. Recovery of the bound fraction by EDTA and anal. by SDS-PAGE revealed two glycoproteins with apparent mol. wts. of 180,000 and 117,000. These were identified immunol. by Western blotting as the .alpha. and .beta. subunits of integrin .alpha.1.beta.1. This report therefore indicates that integrin .alpha.1.beta.1 is a putative type IV collagen receptor of liver parenchymal cells.

L7 ANSWER 46 OF 46 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1991:243107 CAPLUS
DN 114:243107
TI An abundant chick gizzard integrin is the avian .alpha.1.beta.1 integrin heterodimer and functions as a divalent cation-dependent collagen IV receptor
AU Syfrig, Josef; Mann, Karlheinz; Paulsson, Mats
CS Biocent., Univ. Basel, Basel, CH-4056, Switz.
SO Experimental Cell Research (1991), 194(2), 165-73
CODEN: ECREAL; ISSN: 0014-4827
DT Journal
LA English
AB The .alpha.-subunit of an abundant chick gizzard integrin was isolated and fragmented by proteolytic digestion. The N-terminal sequences of the intact polypeptide and of several internal peptides were detd. and were found to be highly homologous to the mammalian integrin .alpha.1-subunit. Monoclonal antibodies to the chick integrin .beta.1-chain react on immunoblots with the gizzard integrin .beta.-subunit. The chain compn. of the abundant chick gizzard integrin is therefore .alpha.1.beta.1. Polyclonal antibodies to the avian integrin .alpha.1-subunit completely block attachment of embryonic gizzard cells to human and chick collagen IV and partially inhibit attachment to mouse Engelbreth-Holm-Swarm (EHS) tumor laminin. In ELISA-style receptor assays, the isolated .alpha.1.beta.1 integrin bound to human and chick collagen IV and to mouse EHS tumor and chick heart laminin. While the binding to collagen IV was abolished by removal of divalent cations, the binding to laminin was not sensitive to EDTA under the conditions used. Collagen I bound the isolated avian .alpha.1.beta.1 integrin only weakly. As collagen IV was the only extracellular matrix protein for which a consistent, divalent cation-dependent, **binding** to the avian .**alpha**.
1.beta.1 integrin could be
demonstrated in both cellular and mol. assays, it is suggested to be a preferred ligand for this integrin.